

SEQUENCE LISTING

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Corixa Corporation
SmithKline Beecham Biologicals S. A.

<120> HER-2/neu Fusion Proteins

<130> 014058-009810PC

<140> US 09/493,480
<141> 2000-01-28

<150> US 60/117,976
<151> 1999-01-29

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<170> PatentIn Ver. 2.1

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<212> PRT
<213> Homo sapiens

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<223> human HER-2/neu protein

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<223> extracellular domain (ECD)

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<223> intracellular domain (ICD)

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<222> (990)..(1255)
<223> phosphorylation domain (PD)

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<222> (990)..(1048)
<223> fragment of the phosphorylation domain, preferred
portion (delta PD)

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Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
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Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Express Mail No.
EL 827035155 US

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60
 Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80
 Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
 85 90 95
 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
 100 105 110
 Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
 115 120 125
 Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
 130 135 140
 Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
 145 150 155 160
 Leu Cys Tyr Gln Asp Thr-Ile Leu Trp Lys Asp Ile Phe His Lys Asn
 165 170 175
 Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
 180 185 190
 His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
 195 200 205
 Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
 210 215 220
 Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
 225 230 235 240
 Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
 245 250 255
 His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
 260 265 270
 Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
 275 280 285
 Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
 290 295 300
 Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
 305 310 315 320
 Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
 325 330 335
 Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
 340 345 350
 Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
 355 360 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
 370 375 380
 Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
 385 390 395 400
 Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
 405 410 415
 Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
 420 425 430
 Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
 435 440 445
 Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
 450 455 460
 Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
 465 470 475 480
 Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
 485 490 495
 Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
 500 505 510
 Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
 515 520 525
 Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
 530 535 540
 Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
 545 550 555 560
 Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
 565 570 575
 Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
 580 585 590
 Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
 595 600 605
 Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
 610 615 620
 Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
 625 630 635 640
 Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser
 645 650 655
 Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
 660 665 670
 Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
 675 680 685

Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
 690 695 700
 Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
 705 710 715 720
 Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
 725 730 735
 Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
 740 745 750
 Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
 755 760 765
 Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
 770 775 780
 Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
 785 790 795 800
 Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
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 Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
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 Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
 835 840 845
 Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
 850 855 860
 Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
 865 870 875 880
 Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
 885 890 895
 Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
 900 905 910
 Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
 915 920 925
 Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
 930 935 940
 Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
 945 950 955 960
 Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
 965 970 975
 Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
 980 985 990
 Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
 995 1000 1005

Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
 1010 1015 1020
 Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
 1025 1030 1035 1040
 Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly
 1045 1050 1055
 Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Ala Pro Arg
 1060 1065 1070
 Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly
 1075 1080 1085
 Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His
 1090 1095 1100
 Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu
 1105 1110 1115 1120
 Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln
 1125 1130 1135
 Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro
 1140 1145 1150
 Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu
 1155 1160 1165
 Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val
 1170 1175 1180
 Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln
 1185 1190 1195 1200
 Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala
 1205 1210 1215
 Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala
 1220 1225 1230
 Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr
 1235 1240 1245
 Leu Gly Leu Asp Val Pro Val
 1250 1255

<210> 2
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 <212> PRT
 <213> Rattus sp.

<220>
 <223> rat HER-2/neu protein

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 <223> extracellular domain (ECD)

<220>
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 <222> (677)..(1256)
 <223> intracellular domain (ICD)

<220>
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 <223> kinase domain (KD)

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 <223> phosphorylation domain (PD)

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 <222> (991)..(1049)
 <223> fragment of the phosphorylation domain, preferred
 portion (delta PD)

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 Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
 35 40 45
 Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60
 Val Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80
 Gln Gly Tyr Met Leu Ile Ala His Asn Gln Val Lys Arg Val Pro Leu
 85 90 95
 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr
 100 105 110
 Ala Leu Ala Val Leu Asp Asn Arg Asp Pro Gln Asp Asn Val Ala Ala
 115 120 125
 Ser Thr Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg
 130 135 140
 Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro
 145 150 155 160
 Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Phe Arg Lys
 165 170 175
 Asn Asn Gln Leu Ala Pro Val Asp Ile Asp Thr Asn Arg Ser Arg Ala
 180 185 190
 Cys Pro Pro Cys Ala Pro Ala Cys Lys Asp Asn His Cys Trp Gly Glu
 195 200 205

Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly
 210 215 220
 Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln
 225 230 235 240
 Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys
 245 250 255
 Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu
 260 265 270
 Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met His Asn Pro Glu Gly
 275 280 285
 Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr
 290 295 300
 Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn
 305 310 315 320
 Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser
 325 330 335
 Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg
 340 345 350
 Gly Ala Arg Ala Ile Thr Ser Asp Asn Val Gln Glu Phe Asp Gly Cys
 355 360 365
 Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly
 370 375 380
 Asp Pro Ser Ser Gly Ile Ala Pro Leu Arg Pro Glu Gln Leu Gln Val
 385 390 395 400
 Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp
 405 410 415
 Pro Asp Ser Leu Arg Asp Leu Ser Val Phe Gln Asn Leu Arg Ile Ile
 420 425 430
 Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly
 435 440 445
 Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser
 450 455 460
 Gly Leu Ala Leu Ile His Arg Asn Ala His Leu Cys Phe Val His Thr
 465 470 475 480
 Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His
 485 490 495
 Ser Gly Asn Arg Pro Glu Glu Asp Cys Gly Leu Glu Gly Leu Val Cys
 500 505 510
 Asn Ser Leu Cys Ala His Gly His Cys Trp Gly Pro Gly Pro Thr Gln
 515 520 525

Cys Val Asn Cys Ser His Phe Leu Arg Gly Gln Glu Cys Val Glu Glu
530 535 540

Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Ser Asp Lys Arg
545 550 555 560

Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr
565 570 575

Cys Phe Gly Ser Glu Ala Asp Gln Cys Ala Ala Cys Ala His Tyr Lys
580 585 590

Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
595 600 605

Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys
610 615 620

Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu
625 630 635 640

Arg Gly Cys Pro Ala Glu-Gln Arg Ala Ser Pro Val Thr Phe Ile Ile
645 650 655

Ala Thr Val Glu Gly Val Leu Leu Phe Leu Ile Leu Val Val Val Val
660 665 670

Gly Ile Leu Ile Lys Arg Arg Arg Gln Lys Ile Arg Lys Tyr Thr Met
675 680 685

Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser
690 695 700

Gly Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu
705 710 715 720

Leu Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr
725 730 735

Lys Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala
740 745 750

Ile Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile
755 760 765

Leu Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser
770 775 780

Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln
785 790 795 800

Leu Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu His Arg Gly
805 810 815

Arg Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Val Gln Ile Ala Lys
820 825 830

Gly Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala
835 840 845

Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp
850 855 860

Phe Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala
865 870 875 880

Asp Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu
885 890 895

Arg Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr
900 905 910

Val Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro
915 920 925

Ala Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln
930 935 940

Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp
945 950 955 960

Met Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu
965 970 975

Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn
980 985 990

Glu Asp Leu Gly Pro Ser Ser Pro Met Asp Ser Thr Phe Tyr Arg Ser
995 1000 1005

Leu Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr
1010 1015 1020

Leu Val Pro Gln Gln Gly Phe Phe Ser Pro Asp Pro Thr Pro Gly Thr
1025 1030 1035 1040

Gly Ser Thr Ala His Arg Arg His Arg Ser Ser Ser Thr Arg Ser Gly
1045 1050 1055

Gly Gly Glu Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Gly Pro Pro
1060 1065 1070

Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp
1075 1080 1085

Gly Asp Leu Ala Met Gly Val Thr Lys Gly Leu Gln Ser Leu Ser Pro
1090 1095 1100

His Asp Leu Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Leu Pro
1105 1110 1115 1120

Leu Pro Pro Glu Thr Asp Gly Tyr Val Ala Pro Leu Ala Cys Ser Pro
1125 1130 1135

Gln Pro Glu Tyr Val Asn Gln Ser Glu Val Gln Pro Gln Pro Pro Leu
1140 1145 1150

Thr Pro Glu Gly Pro Leu Pro Pro Val Arg Pro Ala Gly Ala Thr Leu
1155 1160 1165

Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp
 1170 1175 1180
 Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Val Pro
 1185 1190 1195 1200
 Arg Glu Gly Thr Ala Ser Pro Pro His Pro Ser Pro Ala Phe Ser Pro
 1205 1210 1215
 Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asn Ser Ser Glu Gln Gly
 1220 1225 1230
 Pro Pro Pro Ser Asn Phe Glu Gly Thr Pro Thr Ala Glu Asn Pro Glu
 1235 1240 1245
 Tyr Leu Gly Leu Asp Val Pro Val
 1250 1255

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 <212> PRT
 <213> Homo sapiens

<220>
 <223> extracellular domain (ECD) of human HER-2/neu

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 20 25 30
 Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
 35 40 45
 Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60
 Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80
 Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
 85 90 95
 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
 100 105 110
 Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
 115 120 125
 Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
 130 135 140
 Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
 145 150 155 160
 Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
 165 170 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
 180 185 190
 His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
 195 200 205
 Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
 210 215 220
 Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
 225 230 235 240
 Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
 245 250 255
 His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
 260 265 270
 Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
 275 280 285
 Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
 290 295 300
 Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
 305 310 315 320
 Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
 325 330 335
 Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
 340 345 350
 Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
 355 360 365
 Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
 370 375 380
 Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
 385 390 395 400
 Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
 405 410 415
 Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
 420 425 430
 Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
 435 440 445
 Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
 450 455 460
 Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
 465 470 475 480
 Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
 485 490 495

Pro Thr His Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr
 115 120 125
 Val Pro Leu Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys
 130 135 140
 Ser Pro Gln Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro
 145 150 155 160
 Pro Ser Pro Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala
 165 170 175
 Thr Leu Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val
 180 185 190
 Lys Asp Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu
 195 200 205
 Thr Pro Gln Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe
 210 215 220
 Ser Pro Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu
 225 230 235 240
 Arg Gly Ala Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn
 245 250 255
 Pro Glu Tyr Leu Gly Leu Asp Val Pro Val
 260 265

<210> 5
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 <212> PRT
 <213> Homo sapiens

<220>
 <223> fragment of the phosphorylation domain, preferred
 portion (delta PD) of human HER-2/neu

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 Arg Ser Leu Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu
 20 25 30
 Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro
 35 40 45
 Gly Ala Gly Gly Met Val His His Arg His Arg
 50 55

<210> 6
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 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fusion protein
of ECD and PD of human HER-2/neu

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20 25 30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275 280 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290 295 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
 305 310 315 320
 Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
 325 330 335
 Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
 340 345 350
 Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
 355 360 365
 Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
 370 375 380
 Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
 385 390 395 400
 Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
 405 410 415
 Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
 420 425 430
 Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
 435 440 445
 Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
 450 455 460
 Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
 465 470 475 480
 Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
 485 490 495
 Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
 500 505 510
 Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
 515 520 525
 Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
 530 535 540
 Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
 545 550 555 560
 Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
 565 570 575
 Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
 580 585 590
 Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
 595 600 605
 Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
 610 615 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
 625 630 635 640
 Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Gln Asn Glu
 645 650 655
 Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
 660 665 670
 Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
 675 680 685
 Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
 690 695 700
 Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly
 705 710 715 720
 Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Ala Pro Arg
 725 730 735
 Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly
 740 745 750
 Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His
 755 760 765
 Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu
 770 775 780
 Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln
 785 790 795 800
 Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro
 805 810 815
 Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu
 820 825 830
 Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val
 835 840 845
 Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln
 850 855 860
 Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala
 865 870 875 880
 Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala
 885 890 895
 Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr
 900 905 910
 Leu Gly Leu Asp Val Pro Val
 915

<210> 7
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 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fusion protein
 of ECD and delta PD of human HER-2/neu

<400> 7

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Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
 35 40 45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
 85 90 95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
 100 105 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
 115 120 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
 130 135 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
 145 150 155 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
 165 170 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
 180 185 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
 195 200 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
 210 215 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
 225 230 235 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
 245 250 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
 260 265 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
 275 280 285
 Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
 290 295 300
 Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
 305 310 315 320
 Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
 325 330 335
 Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
 340 345 350
 Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
 355 360 365
 Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
 370 375 380
 Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
 385 390 395 400
 Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
 405 410 415
 Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
 420 425 430
 Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
 435 440 445
 Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
 450 455 460
 Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
 465 470 475 480
 Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
 485 490 495
 Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
 500 505 510
 Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
 515 520 525
 Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
 530 535 540
 Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
 545 550 555 560
 Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
 565 570 575
 Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
 580 585 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
 595 600 605
 Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
 610 615 620
 Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
 625 630 635 640
 Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Gln Asn Glu
 645 650 655
 Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu
 660 665 670
 Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
 675 680 685
 Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
 690 695 700
 Gly Met Val His His Arg His Arg
 705 710

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 <212> PRT
 <213> Rattus sp.

<220>
 <223> extracellular domain (ECD) of rat HER-2/neu

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 20 25 30
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 35 40 45
 Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60
 Val Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80
 Gln Gly Tyr Met Leu Ile Ala His Asn Gln Val Lys Arg Val Pro Leu
 85 90 95
 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr
 100 105 110
 Ala Leu Ala Val Leu Asp Asn Arg Asp Pro Gln Asp Asn Val Ala Ala
 115 120 125
 Ser Thr Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg
 130 135 140

Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro
145 150 155 160

Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Phe Arg Lys
165 170 175

Asn Asn Gln Leu Ala Pro Val Asp Ile Asp Thr Asn Arg Ser Arg Ala
180 185 190

Cys Pro Pro Cys Ala Pro Ala Cys Lys Asp Asn His Cys Trp Gly Glu
195 200 205

Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly
210 215 220

Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln
225 230 235 240

Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys
245 250 255

Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu
260 265 270

Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met His Asn Pro Glu Gly
275 280 285

Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr
290 295 300

Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn
305 310 315 320

Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser
325 330 335

Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg
340 345 350

Gly Ala Arg Ala Ile Thr Ser Asp Asn Val Gln Glu Phe Asp Gly Cys
355 360 365

Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly
370 375 380

Asp Pro Ser Ser Gly Ile Ala Pro Leu Arg Pro Glu Gln Leu Gln Val
385 390 395 400

Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp
405 410 415

Pro Asp Ser Leu Arg Asp Leu Ser Val Phe Gln Asn Leu Arg Ile Ile
420 425 430

Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly
435 440 445

Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser
450 455 460

Gly Leu Ala Leu Ile His Arg Asn Ala His Leu Cys Phe Val His Thr
 465 470 475 480
 Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His
 485 490 495
 Ser Gly Asn Arg Pro Glu Glu Asp Cys Gly Leu Glu Gly Leu Val Cys
 500 505 510
 Asn Ser Leu Cys Ala His Gly His Cys Trp Gly Pro Gly Pro Thr Gln
 515 520 525
 Cys Val Asn Cys Ser His Phe Leu Arg Gly Gln Glu Cys Val Glu Glu
 530 535 540
 Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Ser Asp Lys Arg
 545 550 555 560
 Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr
 565 570 575
 Cys Phe Gly Ser Glu Ala Asp Gln Cys Ala Ala Cys Ala His Tyr Lys
 580 585 590
 Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
 595 600 605
 Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys
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 Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu
 625 630 635 640
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 645 650

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 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)..(3768)
 <223> human HER-2/neu protein

<220>
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 <222> (1)..(1959)
 <223> extracellular domain (ECD) of human HER-2/neu

<220>
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 <222> (2026)..(3765)
 <223> intracellular domain (ICD) of human HER-2/neu

<220>
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 <222> (2968)..(3765)
 <223> phosphorylation domain (PD) of human HER-2/neu

<220>
 <221> misc_feature
 <222> (2968)..(3144)
 <223> preferred portion of the phosphorylation domain
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<210> 10
<211> 3955
<212> DNA
<213> Rattus norvegicus

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<220>
<223> rat HER-2/neu cDNA

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<220>
<221> CDS
<222> (26)..(3799)
<223> rat HER-2/neu protein

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<220>
<221> misc_feature
<222> (26)..(1990)
<223> extracellular domain (ECD) of rat HER-2/neu

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<220>
<221> misc_feature
<222> (2057)..(3796)
<223> intracellular domain (ICD) of rat HER-2/neu

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<220>
<221> misc_feature
<222> (2188)..(3022)
<223> kinase domain (KD) of rat HER-2/neu

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<220>
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<222> (2999)..(3796)
<223> phosphorylation domain (PD) of rat HER-2/neu

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<220>
<221> misc_feature
<222> (2999)..(3173)
<223> preferred portion of the phosphorylation domain
(delta PD) of rat HER-2/neu

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gttgcggtc ctgcccagtc ctgagaccca cctggacatg ctccgccacc tgtaragg 180
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aggagttttg atccgtggga accctcagct ctgctaccag gacatggttt tgtggaagg 540
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<210> 11
 <211> 3771
 <212> DNA
 <213> Mus sp.

<220>
 <223> mouse HER-2/neu

<400> 11

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<210> 12
 <211> 28
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:5' primer for
 mouse HER-2/neu amplification

<400> 12
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<210> 13
 <211> 31
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:3' primer for
 mouse HER-2/neu amplification

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<210> 14
 <211> 1256
 <212> PRT
 <213> Mus sp.

<220>
 <223> mouse HER-2/neu protein

<400> 14
 Met Glu Leu Ala Ala Trp Cys Arg Trp Gly Phe Leu Leu Ala Leu Leu
 1 5 10 15
 Ser Pro Gly Ala Ala Gly Thr Gln Val Cys Thr Gly Thr Asp Met Lys
 20 25 30
 Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
 35 40 45
 Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60

Leu	Pro	Ala	Asn	Ala	Ser	Leu	Ser	Phe	Leu	Gln	Asp	Ile	Gln	Glu	Val	
65					70					75					80	
Gln	Gly	Tyr	Met	Leu	Ile	Ala	His	Asn	Arg	Val	Lys	His	Val	Pro	Leu	
				85					90					95		
Gln	Arg	Leu	Arg	Ile	Val	Arg	Gly	Thr	Gln	Leu	Phe	Glu	Asp	Lys	Tyr	
			100					105					110			
Ala	Leu	Ala	Val	Leu	Asp	Asn	Arg	Asp	Pro	Leu	Asp	Asn	Val	Thr	Thr	
		115					120					125				
Ala	Ala	Pro	Gly	Arg	Thr	Pro	Glu	Gly	Leu	Arg	Glu	Leu	Gln	Leu	Arg	
		130				135					140					
Ser	Leu	Thr	Glu	Ile	Leu	Lys	Gly	Gly	Val	Leu	Ile	Arg	Gly	Asn	Pro	
145					150					155					160	
Gln	Leu	Cys	Tyr	Gln	Asp	Met	Val	Leu	Trp	Lys	Asp	Val	Leu	Arg	Lys	
				165					170					175		
Asn	Asn	Gln	Leu	Ala	Pro	Val	Asp	Met	Asp	Thr	Asn	Arg	Ser	Arg	Ala	
			180					185					190			
Cys	Pro	Pro	Cys	Ala	Pro	Thr	Cys	Lys	Asp	Asn	His	Cys	Trp	Gly	Glu	
		195					200					205				
Ser	Pro	Glu	Asp	Cys	Gln	Ile	Leu	Thr	Gly	Thr	Ile	Cys	Thr	Ser	Gly	
		210				215					220					
Cys	Ala	Arg	Cys	Lys	Gly	Arg	Leu	Pro	Thr	Asp	Cys	Cys	His	Glu	Gln	
225					230					235					240	
Cys	Ala	Ala	Gly	Cys	Thr	Gly	Pro	Lys	His	Ser	Asp	Cys	Leu	Ala	Cys	
				245					250					255		
Leu	His	Phe	Asn	His	Ser	Gly	Ile	Cys	Glu	Leu	His	Cys	Pro	Ala	Leu	
			260					265					270			
Ile	Thr	Tyr	Asn	Thr	Asp	Thr	Phe	Glu	Ser	Met	Leu	Asn	Pro	Glu	Gly	
		275					280					285				
Arg	Tyr	Thr	Phe	Gly	Ala	Ser	Cys	Val	Thr	Thr	Cys	Pro	Tyr	Asn	Tyr	
		290				295					300					
Leu	Ser	Thr	Glu	Val	Gly	Ser	Cys	Thr	Leu	Val	Cys	Pro	Pro	Asn	Asn	
305					310					315					320	
Gln	Glu	Val	Thr	Ala	Glu	Asp	Gly	Thr	Gln	Arg	Cys	Glu	Lys	Cys	Ser	
				325					330					335		
Lys	Pro	Cys	Ala	Gly	Val	Cys	Tyr	Gly	Leu	Gly	Met	Glu	His	Leu	Arg	
			340					345					350			
Gly	Ala	Arg	Ala	Ile	Thr	Ser	Asp	Asn	Ile	Gln	Glu	Phe	Ala	Gly	Cys	
			355				360					365				
Lys	Lys	Ile	Phe	Gly	Ser	Leu	Ala	Phe	Leu	Pro	Glu	Ser	Phe	Asp	Gly	
		370				375					380					

Asn Pro Ser Ser Gly Val Ala Pro Leu Lys Pro Glu His Leu Gln Val
 385 390 395 400
 Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp
 405 410 415
 Pro Glu Ser Phe Gln Asp Leu Ser Val Phe Gln Asn Leu Arg Val Ile
 420 425 430
 Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly
 435 440 445
 Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser
 450 455 460
 Gly Leu Ala Leu Ile His Arg Asn Thr His Leu Cys Phe Val Asn Thr
 465 470 475 480
 Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His
 485 490 495
 Ser Gly Asn Arg Pro Glu Glu Ala Cys Gly Leu Glu Gly Leu Val Cys
 500 505 510
 Asn Ser Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln
 515 520 525
 Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu
 530 535 540
 Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Arg Gly Lys His
 545 550 555 560
 Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr
 565 570 575
 Cys Tyr Gly Ser Glu Ala Asp Gln Cys Glu Ala Cys Ala His Tyr Lys
 580 585 590
 Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
 595 600 605
 Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys
 610 615 620
 Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu
 625 630 635 640
 Arg Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Val Thr Phe Ile Ile
 645 650 655
 Ala Thr Val Val Gly Val Leu Leu Phe Leu Ile Ile Val Val Val Ile
 660 665 670
 Gly Ile Leu Ile Lys Arg Arg Arg Gln Lys Ile Arg Lys Tyr Thr Met
 675 680 685
 Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser
 690 695 700

Leu Val Pro Gln Gln Gly Phe Phe Ser Pro Asp Pro Ala Leu Gly Thr
 1025 1030 1035 1040
 Gly Ser Thr Ala His Arg Arg His Arg Ser Ser Ala Arg Ser Gly
 1045 1050 1055
 Gly Gly Glu Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Pro Pro
 1060 1065 1070
 Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp
 1075 1080 1085
 Gly Asp Leu Ala Val Gly Val Thr Lys Gly Leu Gln Ser Leu Ser Pro
 1090 1095 1100
 His Asp Leu Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Leu Pro
 1105 1110 1115 1120
 Leu Pro Pro Glu Thr Asp Gly Tyr Val Ala Pro Leu Ala Cys Ser Pro
 1125 1130 1135
 Gln Pro Glu Tyr Val Asn Gln Pro Glu Val Arg Pro Gln Ser Pro Leu
 1140 1145 1150
 Thr Pro Glu Gly Pro Pro Pro Pro Ile Arg Pro Ala Gly Ala Thr Leu
 1155 1160 1165
 Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp
 1170 1175 1180
 Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Ala Pro
 1185 1190 1195 1200
 Arg Ala Gly Thr Ala Ser Gln Pro His Pro Ser Pro Ala Phe Ser Pro
 1205 1210 1215
 Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asn Ser Ser Glu Gln Gly
 1220 1225 1230
 Pro Pro Pro Ser Thr Phe Glu Gly Thr Pro Thr Ala Glu Asn Pro Glu
 1235 1240 1245
 Tyr Leu Gly Leu Asp Val Pro Val
 1250 1255

<210> 15

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:PCR primer
PDM-251

<400> 15

cctgaatcgc gaacccaagt gtgcaccggc ac

32

<210> 16
<211> 33
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:PCR primer
PDM-279

<400> 16
ctggactcga gtcattagcg gtgcctgtgg tgg

33

<210> 17
<211> 32
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:AW028 hECD-PD
sense primer with NcoI site

<400> 17
gggccatggg gagcacccaa gtgtgcaccg gc

32

<210> 18
<211> 31
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:AW029 hECD-PD
antisense primer with XhoI site without stop

<400> 18
gggctcgagc actggcacgt ccagacccag g

31

<210> 19
<211> 35
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:AW038 primer
for site-directed mutagenesis

<400> 19
ggccctcca gcccgatgga cagcaccttc taccg

35

<210> 20
<211> 35
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:AW039 primer
for site-directed mutagenesis

<400> 20
cggtagaagg tgctgtccat cgggctggag gggcc 35

<210> 21
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:AW036 sense
primer with NcoI site

<400> 21
gggccatggg tacccaagtg tgtaccgg 28

<210> 22
<211> 61
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:AW037 antisense
primer with XhoI site

<400> 22
gggctcgagt caatggtgat ggtgatggtg tcatggcaca tccaggccta ggtactcagg 60
g 61

<210> 23
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Ra12.JC05 PCR
fragment

<400> 23
ccgccatggg cacggccgcg tccgataact tcc 33

<210> 24
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Ra12.JC06 PCR
fragment

<400> 24
gcgccatggc ggccgggggt ccctcggcc 29

<210> 25
<211> 30
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:LeIF.JC03 PCR
fragment

<400> 25

cgcccatggc gcagaatgat aagatcgccc

30

<210> 26

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:LeIF.JC04 PCR
fragment

<400> 26

gccccatggc gtcgcgcatg aactttcttcg tc

32

106050 9561850